REMARKS

In accordance with the present invention, there are provided genes encoding neuronal nicotinic acetylcholine receptor subunits and proteins encoded thereby. In particular, the invention relates to a family of novel mammalian neuronal nicotinic acetylcholine receptor subunits, for example, the beta2 subunit, which is a non-agonist binding subunit. The invention receptor subunit genes and the protein encoded thereby can be used for a variety of applications, *e.g.*, for drug design and screening. Moreover, the transformed cell lines expressing specific receptor subunits can be produced in quantity for reproducible quantitative analysis of the effects of drugs on receptor functions.

By the present communication, claims 5-6, 8-12 and 14-33 have been cancelled and replaced by new claims 34-44. The newly added claims are presented to define Applicants' invention with great particularity. The new claims do not introduce new matter or require a new search as they are fully supported by the specification and original claims. Applicants respectfully submit that the foregoing amendments substantially reduce the number of claims for consideration (from 26 claims to 12 claims), and place the instant application in condition for allowance or, at a minimum, in better form for appeal. Entry of the amendments at this time is, therefore, respectfully submitted to be proper. Accordingly, entry of the claims submitted herewith is respectfully requested. Upon entry of the amendments submitted herewith, claims 7 and 34-44 will be pending. These claims are attached hereto in Appendix A. The allowance of claim 7 is acknowledged with appreciation.

Drawings

The drawings were objected to as allegedly failing to meet the requirements of 37 C.F.R. §1.84(U)(1), for reasons of record in section 2 of Paper No. 6. Formal drawings are provided herewith and are respectfully submitted to overcome this objection.

Election/Restrictions

Applicants respectfully disagree with the withdrawal of claims 28-30 and 33 from consideration, because these claims are allegedly independent or distinct from the invention

originally claimed (Paper No. 9, page 2). Claims 28-30 and 33 are drawn to nucleic acid probes and/or non-coding nucleic acid derived from the nucleotide sequence of the invention DNA as originally claimed, *i.e.*, sequences shown in Figures 7B(1)-(3) and Figure 8 (sequence for beta2 subunit shown in Figure 8 is the same as that shown in Figures 7B(1)-(3)). Therefore, these claims are interrelated and a prior art search of one would, of necessity, involve a search of the others. However, in an effort to reduce the issues, claims 28-30 and 33 have been cancelled, rendering the restriction moot.

Objection to claim 16

Applicants respectfully disagree with the Examiner's assertion that claim 16 is allegedly in improper dependent form. See Paper No. 9, page 3. It is respectfully submitted that claim 16 is a proper dependent claim of claim 5 because it is directed to a substantially pure RNA that is complementary to the DNA defined by claim 5. However, in an effort to reduce the issues and advance prosecution of the application, claim 16 has been canceled. It is respectfully submitted that the objection is not applicable to newly added claim 38 because RNA is a subset of the subject matter embraced by claim 34, *i.e.*, a polynucleotide. Accordingly, reconsideration and withdrawal of the objection is respectfully requested.

Rejections Under 35 U.S.C. §112, First Paragraph (Written Description)

The rejection of claims 5, 8, 9, 11, 12 and 14 to 27, 31 and 32 under 35 U.S.C. §112, first paragraph, as allegedly being drawn to subject matter lacking adequate written description in the specification, is respectfully traversed.

Applicants respectfully disagree with the Examiner's assertion that the instant claims are allegedly not drawn to a 'neuronal nicotonic acetylcholine receptor beta2 subunit', but only to an isolated nucleic acid presented in Figure 7 (Paper No. 9, pages 3-4). As noted in Applicants' previous response, filed 04/19/02, the written description requirement does not require that a structure be named. Applicants' specification provides substantial written description of biochemical features, including structural and functional properties of invention beta2 subunits of neuronal nicotinic acetylcholine receptors (See Applicants' response filed 04/19/02, pages 7-8).

Nevertheless, in an effort to reduce the issues and advance prosecution of the application, these claims have been cancelled. It is respectfully submitted that the rejection is not applicable to the newly added claims since the invention beta2 subunit of nAChR has been defined by reference to both structural and functional features thereof.

For example, claim 34 characterizes the invention beta2 subunit of nAChR by reference to both its structure (*e.g.*, sequences having a defined level of homology with respect to Figure 7) and function (*e.g.*, various functional properties recited in the claims); claim 39 defines the invention beta2 subunit by reference to both its structure (*e.g.*, hybridizes to the sequence shown in Figure 7) and function (*e.g.*, various functional properties recited in the claims); and claim 42 defines the invention beta2 subunit by reference to both its structure (*e.g.*, sequence having a defined level of homology with respect to other nAChR subunits) and function (*e.g.*, various functional properties).

With respect to claim 11, Applicants disagree with the Examiner's assertion that the limitation "having greater than about 68% sequence homology" allegedly lacks support in the specification. The Examiner's attention is directed to the specification, page 123, Table 8, in which the percent amino acid sequence identity among other nAChR subunits is shown. According to the data shown in the table, the amino acid sequence identity among nAChR subunits is less than 68%. Therefore, these data in the specification fully support the requirement recited in claim 11. However, in an effort to reduce the issues and advance prosecution, claim 11 has been canceled, rendering the rejection moot.

Accordingly, reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. §112, first paragraph, is respectfully requested.

Rejections Under 35 U.S.C. §112, Second Paragraph (Indefiniteness)

The rejection of claims 5, 6, 8, 9, 11, 12, 14, 16 to 27, 31 and 32 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite is respectfully traversed.

Applicants disagree with the Examiner's assertion that claims 5, 6, 12, 14 to 24, 26, 27, 31 and 32 are allegedly indefinite because there is no antecedent basis for "the sense strand". The language used in these claims is clear. However, in an effort to reduce the issues and advance prosecution, the term "the sense strand" has been omitted in the newly added claims. Therefore, the rejection is not applicable to the newly added claims.

In addition, Applicants respectfully disagree with the Examiner's assertion that claims 5, 6, 8, 9, 11, 12, 14 to 27, 31 and 32 are allegedly indefinite because the term "beta2 subunit" is allegedly not defined in the instant specification as exclusive to a protein encompassed by the term "beta2", having that property or combination of properties, which is unique to beta2 subunit. Paper No. 9, pages 4-5.

It is respectfully submitted that the term "beta2 subunit" is clear when read in light of the specification. Those skilled in the art, especially those with high level of skill in the art, readily understand the meaning of the term "beta2 subunit" as it has long been used in the art based on the well known pharmacological properties thereof.

Moreover, as stated above, newly submitted claim 34 characterize the invention beta2 subunit of nAChR by reference to both its structure (*e.g.*, sequences having a defined level of homology with respect to Figure 7) and function (*e.g.*, various functional properties recited in the claims); similarly, claim 39 defines the invention beta2 subunit by reference to both its structure (*e.g.*, hybridizes to the sequence shown in Figure 7) and function (*e.g.*, various functional properties recited in the claims); and likewise, claim 42 defines the invention beta2 subunit by reference to both its structure (*e.g.*, having a defined level of sequence homology with respect to other nAChR subunits) and function (*e.g.*, various functional properties). Therefore, the rejection is not applicable to the newly submitted claims.

Furthermore, Applicants respectfully disagree with the Examiner's assertion that claims 15, 25 to 27 are allegedly indefinite "because the limitation 'under stringent conditions' is conditional and no single specific set of conditions which define this limitation are recited in either the claims or the specification."

The claims should be read in light of the specification. As noted in Applicants' specification, hybridization methods are well known to those skilled in the art (see specification page 24, lines 15-20). Exemplary teachings of hybridization procedures and conditions are recited in the specification (see page 68, lines 3-20; page 52, line 19 to page 53, line 1). Therefore, the term "under stringent conditions" as consistently used throughout Applicants' specification, the claims and in the art is respectfully submitted to be clear to those skilled in the art.

Moreover, Applicants respectfully disagree with the Examiner's assertion that claims 22 and 24 are allegedly indefinite, because it is allegedly unclear which "neuronal nicotinic acetylcholine receptor alpha subunits" the claims are referring to. It is respectfully submitted to be clear to those skilled in the art when read in light of the specification that the claims are referring to neuronal nicotinic acetylcholine receptor alpha subunits, *i.e.*, alpha2, alpha3, alpha4 and alpha5. Nevertheless, in an effort to reduce the issues and advance prosecution of the application, these claims have been cancelled. The rejection is not applicable to new claim 42 because the claim specifically provides that the neuronal nicotinic acetylcholine receptor alpha subunits are selected from the group consisting of alpha 2, alpha 3, alpha 4 and alpha 5.

Accordingly, since the newly submitted claims fully satisfy the requirements of 35 U.S.C. §112, second paragraph, reconsideration and withdrawal of this rejections are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, the present application is respectfully submitted to be in condition for allowance. Accordingly, reconsideration and favorable action with respect to the pending claims is respectfully requested. In the event any issues remain to be resolved in view of this communication, the Examiner is invited to contact the undersigned at the number given below so that a prompt disposition of this application can be achieved.

Respectfully submitted,

Date 10/3/02

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Enclosures: Appendix A;
Formal Drawings

APPENDIX A – Claims Requested to Enter for Examination

7 (Reiterated). Substantially pure DNA having the protein coding region of the nucleotide sequence shown in Figures 7B(1), 7B(2), and 7B(3).

34 (New). A substantially pure polynucleotide comprising DNA encoding a beta2 subunit of a neuronal acetylcholine receptor, wherein said DNA has greater than 64% sequence homology to the nucleotide sequence set forth in Figures 7B(1), 7B(2) and 7B(3), and

wherein said beta2 subunit has one or more functional properties selected from the group consisting of:

i) being able to substitute for the muscle beta1 subunit in the formation of an acetylcholine receptor, but not being able to substitute for the gamma or delta subunit of a neuronal nicotinic acetylcholine receptor;

ii) not binding acetylcholine, nicotine or analogs thereof;

iii) forming, in conjunction with an alpha3 or an alpha4 subunit, a neuronal nicotinic acetylcholine receptor that is blocked by bungarotoxin 3.1 but not by α-bungarotoxin; and

iv) forming, in conjunction with an alpha2 subunit, a neuronal nicotinic acetylcholine receptor that is not blocked by either bungarotoxin 3.1 or α-bungarotoxin.

35 (New). The substantially pure DNA of claim 34 comprising the nucleotide sequence of pPCX49, ATCC No. 67643, or complement thereof.

36 (New). Cells transformed by the substantially pure DNA of claim 34.

37 (New). A vector containing the substantially pure DNA of claim 34.

38 (New). A RNA complementary to said polynucleotide of claim 34.

39 (New). A substantially pure polynucleotide encoding a beta2 subunit of a neuronal acetylcholine receptor, wherein said polynucleotide has at least 15 contiguous bases that hybridize under stringent conditions to the complement of the nucleotide sequence set forth in Figures 7B(1), 7B(2) and 7B(3),

wherein said beta2 subunit has one or more functional properties selected from the group consisting of:

i) being able to substitute for the muscle beta1 subunit in the formation of an acetylcholine receptor, but not being able to substitute for the gamma or delta subunit of a neuronal nicotinic acetylcholine receptor;

ii) not binding acetylcholine, nicotine or analogs thereof;

iii) forming, in conjunction with an alpha3 or an alpha4 subunit, a neuronal nicotinic acetylcholine receptor that is blocked by bungarotoxin 3.1 but not by α-bungarotoxin; and

iv) forming, in conjunction with an alpha2 subunit, a neuronal nicotinic acetylcholine receptor that is not blocked by either bungarotoxin 3.1 or α-bungarotoxin.

40 (New). Cells transformed by the substantially pure polynucleotide of claim 39.

41 (New). A vector containing the substantially pure polynucleotide of claim 39.

42 (New). A substantially pure polynucleotide encoding a neuronal nicotinic acetylcholine receptor beta2 subunit, wherein said beta2 subunit has

a) no greater than 50% amino acid sequence identity to neuronal nicotinic acetylcholine receptor alpha subunits selected from the group consisting of alpha2, alpha3, alpha4 and alpha5;

b) 44% amino acid sequence identity to a beta3 subunit of a neuronal nicotinic acetylcholine receptor; and

c) 64% amino acid sequence identity to a beta4 subunit of a neuronal nicotinic acetylcholine receptor; and

wherein said beta2 subunit has one or more functional properties selected from the group consisting of:

i) being able to substitute for the muscle beta1 subunit in the formation of an acetylcholine receptor, but not being able to substitute for the gamma or delta subunit of a neuronal nicotinic acetylcholine receptor;

ii) not binding acetylcholine, nicotine or analogs thereof;

iii) forming, in conjunction with an alpha3 or an alpha4 subunit, a neuronal nicotinic acetylcholine receptor that is blocked by bungarotoxin 3.1 but not by α-bungarotoxin; and

iv) forming, in conjunction with an alpha2 subunit, a neuronal nicotinic acetylcholine receptor that is not blocked by either bungarotoxin 3.1 or α-bungarotoxin.

43 (New). Cells transformed by the substantially pure polynucleotide of claim 42.

44 (New). A vector containing the substantially pure polynucleotide of claim 42.